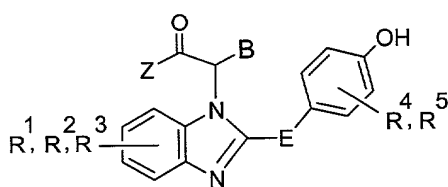
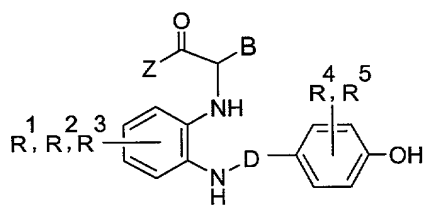
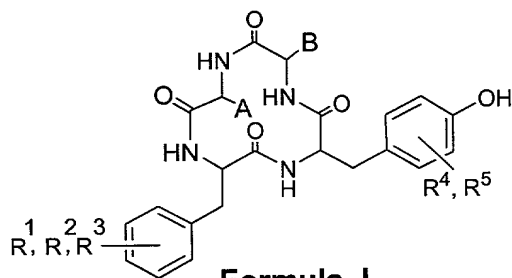


CLAIMS:

1. A compound of general formula I, II or III, or a pharmaceutically acceptable salt thereof:



5 wherein:

A is -hydrogen, -(C₁-C₈)alkyl or -(C₁-C₈)alkyl substituted by hydroxy;

B is -(C₁-C₆)alkylguanidino,
 -(C₁-C₆)alkyl(4-imidazolyl), -(C₁-C₆)alkylamino,
 10 p-aminophenylalkyl (C₁-C₆)-, p-guanidinophenylalkyl (C₁-C₆)- or
 4-pyridinylalkyl (C₁-C₆)-;

D is -(CO)-, -(CO)-(C₁-C₆)alkylene or
 -(C₁-C₆)alkylene;

E is a single bond or -(C₁-C₆)alkylene;

15 Z is -NH₂, -NH-(C₁-C₆)alkylcarboxamide,
 -NH-(C₁-C₆)alkyl, -NH-(N-benzyl), -NH-cyclo(C₅-C₇)alkyl,
 -NH-2-(1-piperidyl)ethyl, -NH-2-(1-pyrrolidyl)ethyl,
 -NH-2-(1-pyridyl)ethyl, -NH-2-(morpholino)ethyl,

-morpholino, -piperidyl, -OH, -(C₁-C₆)alkoxy, -O-benzyl or
-O-halobenzyl;

R¹, R² and R³ are, independent of one another,
-hydrogen, -arylcarbonylamino, -(C₁-C₆)alkoylamino,
5 - (C₁-C₆)alkylamino, -(C₁-C₆)alkyloxy,
-(C₁-C₆)alkylaminocarbonyl, -carboxy, -OH, -benzoyl,
-p-halogenobenzoyl, -methyl, -S-(2,4-dinitrophenyl),
-S-(3-nitro-2-pyridinesulphenyl), -sulfonyl,
-trifluoromethyl, -(C₁-C₆)alkylaminocarbonylamino, -halo or
10 -amino;

R⁴ and R⁵ are, independent of one another,
-hydrogen, -(C₁-C₆)alkyl, -methyloxy, -nitro, -amino,
-arylcarbonylamino, -(C₁-C₆)alkoylamino, -(C₁-C₆)alkylamino,
-halo or -OH.

15 2. A compound according to claim 1, which is a
compound of Formula I or a pharmaceutically acceptable salt
thereof.

3. A compound according to claim 1, which is a
compound of Formula II or a pharmaceutically acceptable salt
20 thereof.

4. A compound according to claim 1, which is a
compound of Formula III or a pharmaceutically acceptable
salt thereof.

5. The compound according to claim 1, or a
25 pharmaceutically acceptable salt thereof, wherein A is
hydrogen, CH₃CH(OH)- or (CH₃)₂CHCH₂-.

6. The compound according to claim 1, or a
pharmaceutically acceptable salt thereof, wherein B is
H₂N-C(NH)-NH-CH₂CH₂CH₂- or H₂N-(CH₂)₄-.

7. A compound according to claim 1 selected from the group consisting of:

Cyclo(-Gly-(p-chloro)Phe-Tyr-D-Arg-) [I-1] (SEQ ID NO. 5);

5 Cyclo(-Gly-(p-chloro)Phe-Tyr-(p-amino)Phe-) [I-2] (SEQ ID NO. 6);

Cyclo(-Gly-(p-chloro)Phe-Tyr-(p-guanidino)Phe-) [I-3] (SEQ ID NO. 7);

Cyclo(-Gly-(p-amino)Phe-Tyr-D-Arg-) [I-4] (SEQ ID NO. 8);

Cyclo(-Thr-(p-chloro)Phe-Tyr-D-Arg-) [I-5] (SEQ ID NO. 9);

10 N-5-guanidinopentanamide-(2S)-yl-2-N-(p-hydroxyphenylacetyl)phenylenediamine [II-1];

N-5-guanidinopentanamide-(2S)-yl-2-N-(p-hydroxyphenylacetyl)-4-trifluoromethyl-phenylenediamine [II-2];

15 N-5-guanidinopentanamide-(2R)-yl-2-N-(p-hydroxyphenylacetyl)-4-carboxy-phenylenediamine [II-3];

N-5-guanidinopentanamide-(2R)-yl-2-N-(p-hydroxyphenylacetyl)-4-(p-chlorobenzoyl)-phenylenediamine [II-4]; and,

20 N-5-guanidinopentanamide-(2R)-yl-2-(p-hydroxybenzyl)-5-carboxybenzimidazole [III-1].

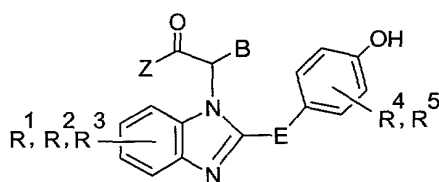
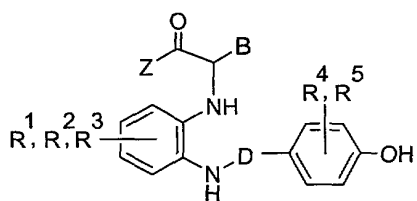
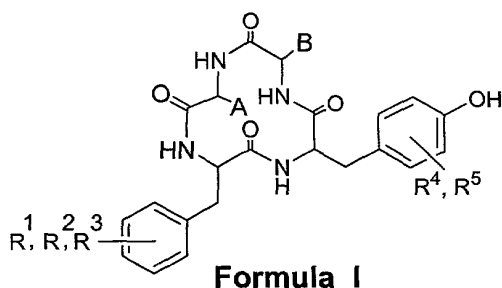
8. A pharmaceutical composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, in admixture with morphine.

25 9. A pharmaceutical composition comprising a compound according to claim 7, or a pharmaceutically acceptable salt thereof, in admixture with morphine.

10. A pharmaceutical composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable carrier, diluent or excipient.

5 11. A pharmaceutical composition comprising a compound according to claim 7, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable carrier, diluent or excipient.

12. A method of inhibiting induction of
10 cyclooxygenase-2 (COX-2) in an animal comprising the step of administering to the animal an effective amount of a compound of general formula I, II or III, or a pharmaceutically acceptable salt thereof:



15 wherein:

A is -hydrogen, -(C₁-C₈)alkyl or -(C₁-C₈)alkyl substituted by hydroxy;

B is -(C₁-C₆)alkylguanidino,
-(C₁-C₆)alkyl(4-imidazolyl), -(C₁-C₆)alkylamino,

p-aminophenylalkyl (C₁-C₆)-, p-guanidinophenylalkyl (C₁-C₆)- or 4-pyridinylalkyl (C₁-C₆)-;

D is -(CO)-, -(CO)-(C₁-C₆)alkylene or -(C₁-C₆)alkylene;

5 E is a single bond or -(C₁-C₆)alkylene;

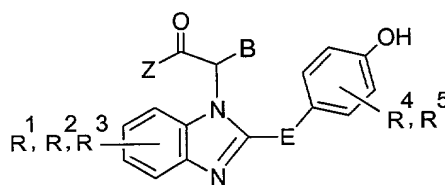
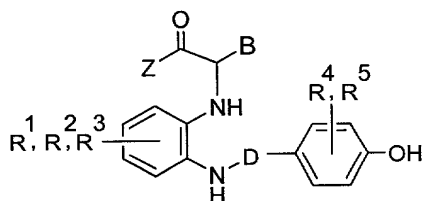
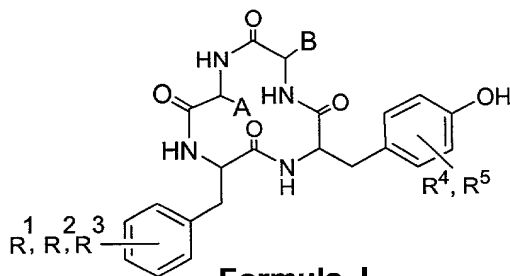
Z is -NH₂, -NH-(C₁-C₆)alkylcarboxamide, -NH-(C₁-C₆)alkyl, -NH-(N-benzyl), -NH-cyclo(C₅-C₇)alkyl, -NH-2-(1-piperidyl)ethyl, -NH-2-(1-pyrrolidyl)ethyl, -NH-2-(1-pyridyl)ethyl, -NH-2-(morpholino)ethyl, 10 -morpholino, -piperidyl, -OH, -(C₁-C₆)alkoxy, -O-benzyl or -O-halobenzyl;

R¹, R² and R³ are, independent of one another, -hydrogen, arylcarbonylamino, -(C₁-C₆)alkoylamino, -(C₁-C₆)alkylamino, -(C₁-C₆)alkyloxy, 15 -(C₁-C₆)alkylaminocarbonyl, -carboxy, -OH, benzoyl, -p-halogenobenzoyl, -methyl, -S-(2,4-dinitrophenyl), -S-(3-nitro-2-pyridinesulfonyl), -sulfonyl, -trifluoromethyl, -(C₁-C₆)alkylaminocarbonylamino, -halo or -amino;

20 R⁴ and R⁵ are, independent of one another, -hydrogen, -(C₁-C₆)alkyl, -methyloxy, -nitro, -amino, -arylcarbonylamino, -(C₁-C₆)alkoylamino, -(C₁-C₆)alkylamino, -halo or -OH.

13. The method according to claim 12, wherein the 25 compound is administered centrally or peripherally.

14. A method of managing pain in an animal comprising the step of administering to the animal an effective amount of a compound of general formula I, II or III, or a pharmaceutically acceptable salt thereof:



wherein:

A is hydrogen, $-(C_1-C_8)$ alkyl or $-(C_1-C_8)$ alkyl substituted by hydroxy;

B is $-(C_1-C_6)$ alkylguanidino, $-(C_1-C_6)$ alkyl (4-imidazolyl), $-(C_1-C_6)$ alkylamino, p-aminophenylalkyl $(C_1-C_6)-$, p-guanidinophenylalkyl $(C_1-C_6)-$ or 4-pyridinylalkyl $(C_1-C_6)-$;

D is $-(CO)-$, $-(CO)-(C_1-C_6)$ alkylene or $-(C_1-C_6)$ alkylene;

E is a single bond or $-(C_1-C_6)$ alkylene;

Z is $-NH_2$, $-NH-(C_1-C_6)$ alkylcarboxamide, $-NH-(C_1-C_6)$ alkyl, $-NH-(N-benzyl)$, $-NH-cyclo(C_5-C_7)$ alkyl, $-NH-2-(1-piperidyl)ethyl$, $-NH-2-(1-pyrrolidyl)ethyl$, $-NH-2-(1-pyridyl)ethyl$, $-NH-2-(morpholino)ethyl$, morpholino, piperidyl, $-OH$, $-(C_1-C_6)$ alkoxy, $-O-benzyl$ or $-O-halobenzyl$;

R^1 , R^2 and R^3 are, independent of one another, hydrogen, arylcarbonylamino, $-(C_1-C_6)$ alkoylamino,

$-(C_1-C_6)$ alkylamino, $-(C_1-C_6)$ alkyloxy,

- (C₁-C₆)alkylaminocarbonyl, -carboxy, -OH, benzoyl,
-p-halogenobenzoyl, -methyl, -S-(2,4-dinitrophenyl),
-S-(3-nitro-2-pyridinesulfenyl), -sulfonyl,
-trifluoromethyl, -(C₁-C₆)alkylaminocarbonylamino, -halo or
5 -amino;

R⁴ and R⁵ are, independent of one another,
-hydrogen, -(C₁-C₆)alkyl, -methyloxy, -nitro, -amino,
-arylcarbonylamino, -(C₁-C₆)alkoylamino, -(C₁-C₆)alkylamino,
-halo or -OH.

10 15. The method according to claim 14, wherein the
compound is administered centrally or peripherally.

16. The method according to claim 15, wherein the
compound is administered in conjunction with morphine.

15 17. The method according to claim 15, wherein the
compound is administered for veterinary purposes.

18. The method according to claim 16, wherein the
compound is administered for veterinary purposes.